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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/774,887	02/09/2004	Angel Lopez	A20-017DIV	8791

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COLEMAN SUDOL SAPONE, P.C.
714 COLORADO AVENUE
BRIDGE PORT, CT 06605-1601

EXAMINER	
MERTZ, PREMA MARIA	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 09/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/774,887	LOPEZ ET AL.	
	Examiner	Art Unit	
	Prema M. Mertz	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 32-39 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 32-39 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 2/9/04.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group 4 (claims 34-35, 38-39) in the reply filed on 8/15/2006 is acknowledged. The traversal is on the ground(s) that the examination of all 4 Groups would not constitute an undue burden on the Examiner because the same active material, namely the monoclonal antibody was used in all the 4 methods and the target cells were either eosinophil or leukaemic cells and a search for one type of cell in the claimed method would reveal art regarding the other type of cell. This argument is found persuasive. The restriction requirement is being withdrawn and all 4 Groups will be examined in the instant application.

Claims 32-39 are pending and under consideration by the Examiner.

Specification

2. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. It is suggested that the title be amended to recite a method using the monoclonal antibody.

Claim objections

3a. Claims 32-33 are objected to under 37 CFR 1.75 as being a substantial duplicate of claims 36-37. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

3b. Claims 34-35 are objected to under 37 CFR 1.75 as being a substantial duplicate of claims 38-39. When two claims in an application are duplicates or else are so close in content

that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 112, first paragraph, non-enablement

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4a. Claim 32-39 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for (i) a method of inhibiting IL-5, IL-3 or GM-CSF mediated leukaemic cell proliferation *in vitro* by contacting the leukaemic cells with monoclonal antibody BION-1 or fragments thereof capable of inhibiting the binding of cytokines lL-3, GM-CSF and IL-5 to the common receptor βc, wherein the monoclonal antibody BION-1 or fragments thereof binds to both the B'-C' loop and the F'-G' of domain 4 of the βc subunit, and (ii) a method of inhibiting IL-5, IL-3 or GM-CSF mediated eosinophil activation, eosinophil production or eosinophil survival *in vitro*, by contacting the eosinophils with monoclonal antibody BION-1 or fragments thereof capable of inhibiting the binding of cytokines lL-3, GM-CSF and IL-5 to the common receptor βc, wherein the monoclonal antibody BION-1 or fragments thereof binds to both the B'-C' loop and the F'-G' of domain 4 of the βc subunit does not reasonably provide enablement for these methods *in vivo*. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The claims are drawn very broadly to methods of inhibiting *in vitro* and *in vivo* the IL-5, IL-3 or GM-CSF mediated eosinophil activation, eosinophil production and eosinophil survival (see pages 20-22) and inhibiting the IL-5, IL-3 or GM-CSF mediated effects on leukaemic cells (see page 22, lines 11-17). However, the specification fails to provide any guidance for the successful inhibition of any specific conditions by administering the BION antibody to patients to treat a particular condition. Resolution of the various complications in regards to using any given antibody that is immunoreactive for any given protein as a therapeutic agent is highly unpredictable. One of skill in the art would have been unable to practice the invention without engaging in undue trial and error experimentation. In order to practice the invention using the specification and the state of the art as outlined below, the quantity of experimentation required to practice the invention as claimed *in vivo* would require the *de novo* determination of pharmaceutical formulations of antibody that is immunoreactive as a therapeutic agent with known antibodies against known proteins with signs, and symptoms to correlate with inhibition of the target protein. In the absence of any guidance from the specification, the amount of experimentation would be undue, and one would have been unable to practice the invention over the scope claimed.

Furthermore, the specification is non-enabling for a method of treating a disease involving cytokines IL-5, IL-3 or GM-CSF in a patient by administering BION-1 antibody because to practice such a method would require knowledge of the route, duration and quantity of administration of that antibody to a subject for the diseases involving the cytokines, and this information is not provided by the instant specification. The instant specification clearly fails to supply the guidance that would be needed by a routine practitioner. The instant specification has also failed to disclose how these parameters are to be determined, how a similar method was practiced in the art with a different

agent or to provide even a single working example, prophetic or actual of the claimed method. In the absence of this guidance, a practitioner would have to resort to a substantial amount of undue experimentation involving the variation in the amount and duration of administration of the proteins of the instant invention and in determining a suitable route of administration. The instant situation is directly analogous to that which was addressed in In re Colianni, 195 U.S.P.Q. 150, C.A.F.C., which held that a "disclosure that calls for application of 'sufficient' ultrasonic energy to practice claimed method of fusing bones but does not disclose what 'sufficient' dosage of ultrasonic energy might be or how those skilled in the art might select appropriate intensity, frequency, and duration, and contains no specific examples or embodiment by way of illustration of how claimed method is to be practiced does not meet requirements of 35 U.S.C. § 112 first paragraph".

The specification as filed does not provide any guidance or examples that would enable a skilled artisan to use the disclosed methods of using the BION-1 antibody that is immunoreactive and a therapeutic agent in a patient. Additionally, a person skilled in the art would recognize that predicting the efficacy of using a given antibody that is immunoreactive for a protein as a therapeutic agent *in vivo* based solely on *prophetic suggestion* as highly problematic (see MPEP §2164.02). Thus, although the specification discloses a method of contacting cells *in vitro* with the BION-1 antibody (see pages 18-21), the specification fails to disclose methodologies of using the BION-1 antibody as a therapeutic agent, and such a disclosure would not be considered enabling since the state of protein aggregation and passive immunization as highly unpredictable. The factors listed below have been considered in the analysis of enablement [see MPEP §2164.01(a) and *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)]:

(A) The breadth of the claims;
(B) The nature of the invention;
(C) The state of the prior art;

(D) The level of one of ordinary skill;
(E) The level of predictability in the art;
(F) The amount of direction provided by the inventor;
(G) The existence of working examples; and
(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The following references are cited herein to illustrate the state of the art for treatment of specific conditions with antibodies.

On the nature of passive immunization, Fox *et al.* (1997) teaches that the recent success of "biologic" agents (i.e. anti-TNF antibody and TNF receptors) in rheumatoid arthritis and of intravenous gamma globulin in various autoimmune disease suggests a potential role for these agents after "controlled trials" have been performed (see page 396, column 1, last 5 lines).

Molina et al. (1996) teach that intravenous immunoglobulin therapy has been utilized in the treatment of sensory neuropathy associated with Sjogren's syndrome.

Canhao et al. (2000) teach that intravenous gammaglobulin may be useful in the treatment of autoimmune disease (see column 2, second full para).

Claim Rejections - 35 USC § 112, second paragraph

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 32-39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 32-39 are rejected as vague and indefinite for several reasons.

Claims 32-39 are vague and indefinite because the claims recite a method but there are no steps recited in the method. Furthermore, the claims fail to recite a condition to be treated. The claims merely recite an activity of the monoclonal antibody.

Claims 32-39 are vague and indefinite because they fail to recite a specific condition to be treated. For example, in claim 34, recitation of "eosinophil activation or survival" encompasses conditions such as allergy or asthma.

Conclusion

No claim is allowed.

Claims 32-39 are rejected.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Prema Mertz whose telephone number is (571) 272-0876. The examiner can normally be reached on Monday-Friday from 7:00AM to 3:30PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached on (571) 272-0835.

Official papers filed by fax should be directed to (571) 273-8300. Faxed draft or informal communications with the examiner should be directed to (571) 273-0876.

Information regarding the status of an application may be obtained from the Patent application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Prema Mertz

Prema Mertz Ph.D., J.D.
Primary Examiner
Art Unit 1646
September 21, 2006